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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,616	01/02/2002	Priscilla Anne Furth	08830-002003	7943

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EXAMINER	
KETTER, JAMES S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,616	FURTH ET AL.	
	Examiner	Art Unit	
	James S. Ketter	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *13-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892).
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Group I, claims 1-12 and 19-21 in Paper No. 6, filed 1 August 22002 is acknowledged. The traversal is on the ground(s) that no search burden would exist to serch for the apparatus once a search for the method of using the apparatus has been made. This is not found persuasive because the apparatus might be found for use in a different method, and the search for the elected method would necessarily be performed to find the claimed method.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12 and 19-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 112 of U.S. Patent No. 5,998,382.

Although the conflicting claims are not identical, they are not patentably distinct from each other because, with respect to instant claim 1, the instant claim encompasses the patented claim. With respect to instant claims 2-12 and 19-21, an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). The instant claims in each instance are more narrowly drawn than the patented claim. However, the portion of the disclosure of US Patent 5,998,382 that supports patented claim 12 sets forth the limitations of instant claims 2-12 and 19-21. Therefore, it would have been obvious to have practiced the method of patented claim 12 within the limitations recited in instant claims 2-12 and 19-21.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of gene transfer for non-therapeutic purposes and for genetic immunization, i.e., vaccination with a composition comprising a nucleic acid segment which expresses the antigen of interest, does not reasonably provide enablement for methods of gene therapy other than genetic immunization, i.e., embodiments encompassed by steps from groups "(a)", "(b)", "(c)" and "(j)", nor for generation of a transgenic organism, i.e.,

embodiments encompassed by steps from group "(e)". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The following factors have been considered in the rejection with respect to gene therapy:

The nature of the invention. The claimed invention encompasses a gene therapy method, i.e., methods wherein the cells are transfected with a recombinant gene, and as such, the method must be therapeutically useable to be enabled.

The amount of direction or guidance presented in the specification, and the presence or absence of working examples.

The specification as filed teaches that some expression of a reporter gene construct is seen after injection into mice or sheep, near the injection site. However, no actual showing of successful treatment of a defect is exemplified. Further, the actual level of expression of the reporter gene was not shown to be therapeutically useful, i.e., sufficient and predictable, nor was any determination of the persistence of expression made and disclosed. A brief listing of potentially useful expression vectors that might be employed in the disclosed system is set forth at the first paragraph of page 9 of the specification. However, no discussion of what levels of expression of any promoters is offered. Furthermore, no teachings with respect to the use of any particular expressed protein for any particular disease state, are set forth. These factors would have to be determined by trial-and-error methodology.

The state of the prior art, and the predictability or unpredictability of the art. Generally, the prior art had seen no successes in treatment methods of either the in vivo or the ex vivo type of gene therapy. Several reviews of the art are discussed below, which show that the problems

of vector selection and, more importantly, persistence of predictable and useable levels of expression of the therapeutic protein, represented technical barriers to the practice of gene therapy methods. Both references, it should be noted, were published after the effective filing date of the claimed invention. Verma et al. (U, newly cited) teaches, e.g., at the four paragraphs at page 240, starting with the paragraph bridging the left-hand and center columns, and ending with the second full paragraph at the right-hand column, that persistence of expression and adequate expression systems, i.e., enhancer-promoter combinations, were problematic in gene therapy methods tried through that time. Furthermore, Table 2, at page 242, shows that none of the transfection systems extant at the time were suitable for actual treatment methods. Anderson (V, newly cited) sets forth the state of the art as of 1998. Specifically, Anderson makes clear that methods extant in the art, particularly vector selection, delivery methods and persistence of gene expression, were still inadequate to permit routine practice of the gene therapy, let alone any demonstrably successful practice at all. Both the first paragraph, left-hand column, at page 25 and the conclusory paragraphs at page 30 make clear that Anderson did not regard practice of gene therapy methods at all routine as of 1998.

The quantity of experimentation. It is clear from the art, as shown by Verma et al. or Anderson, cited above, that a very large amount experimentation had already been underway in the art as of 1997 and 1998. Even with that amount of work, no successful gene therapy methods had been demonstrated. Both references acknowledge the need for more work as of those dates. See, e.g., Verma et al. at page 239, at the first two introductory paragraphs, and Anderson, e.g., at page 25, also at the first two introductory paragraphs, and the last two paragraphs at page 30.

The breadth of the claims. The instant claims are drawn to the treatment of a wide variety of disease states, and to a wide variety of protein to be expressed in such treatment. As such, the claims would have been regarded by one of skill as very broad.

Conclusion. Were the skilled practitioner to have attempted to practice the claimed gene therapy methods, said practitioner first would have turned first to the specification for guidance in selecting dosages, treatment regimens and other factors which may bear upon the success of such treatment. However, as set forth above, such guidance in the specification is limited in nature, and is insufficient with respect to prediction of proper levels of expression. Said practitioner then would have turned to the prior art to obtain detailed guidance for practice of the claimed methods. However, as set forth above, the prior art does not recognize any clearly successful gene therapy methods. Thus, the skilled practitioner would not have been able to find the necessary guidance in the prior art. Finally, said practitioner would have been forced to turn to empirical experimentation to determine appropriate dosages, treatment regimens and other factors, required for successful practice of a gene therapy method. However, as set forth above, the amount of experimentation recognized by the art as required for development of a successful gene therapy protocol is very large, and of a largely trial-and-error nature. Furthermore, as set forth above, the field of gene therapy is unpredictable. A large amount of experimentation in an unpredictable art with little or no available guidance is clearly undue experimentation.

With respect to methods of generating transgenic organisms using the claims method, it is noted that the instant claims are limited to administering plasmid to somatic tissues, particularly skin, muscle, fat and mammary tissues. A transgenic organism, i.e., transgenic animal, has the genetic construct incorporated, at latest, in the fertilized ovum, leading to the presence of the

genetic material in all cells. The method suggested by "(e)" would give rise to a "chimeric" organism. Placement of nucleic acid into differentiated somatic cells simply will not lead to the subject becoming "transgenic".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 19, and therefore 2-12 and 20 that depend therefrom, and claim 21, recite "expressed in a living organism". However, the expression occurs in the recited organism, and therefore the phrase should read "expressed in the living organism".

Claims 1 and 19, and therefore 2-12 and 20 that depend therefrom, are drawn to a method of causing "transient gene expression" and "stable gene expression". Since it does not appear from the specification that both necessarily occur upon practice of the method, it would appear that "or" was intended in place of "and".

Claims 1 and 19, and therefore 2-12 and 20 that depend therefrom, as well as claim 21, recite "tissue of living organisms" where the singular "tissue of a living organism" is clearer. The plural implies that the method must be practiced on plural subjects.

Claims 1 and 19 and therefore 2-12 and 20 that depend therefrom, are drawn to a method reciting "administering…through a jet injector technique". However, this phrase is vague, as it

is not clear what steps might be encompassed by a "jet injector technique". It is suggested that language mirroring that in claim 1 of US Patent 5,998,382, i.e., "comprising...administering... using a jet injector" would clarify the claims.

Claim 2, and therefore claims 3 and 6 that depend therefrom, recites "further involving the steps of a member selected from" the recited group. However, "the steps" refers to an undisclosed set of method steps, and as such, is not defined.

Claim 2, and therefore claims 3 and 6 that depend therefrom, recites "bio-reactors". However, a bioreactor is understood in the art to be an apparatus which contains cells. However, it is not clear if Applicants intended that an apparatus be involved in the instant claims.

Claim 2, and therefore claims 3 and 6 that depend therefrom, recites "transgenic" in reference to organisms. However, as noted in the rejection under 35 USC § 112, first paragraph, above, it would appear that the term "chimeric" or its equivalent was intended, as the recited method could not give rise to a fully transgenic organism, e.g., transgenic animal.

In claim 5, "components", signals" and "sequences" should be in the singular, as apparently only one of each is employed in each DNA sequence.

Further in claim 5, it would appear that "coating" should be "coding".

Claims 5 and 6 recite the term "specific" in several instances. However, the use of "specific" in this context implies some limitation of that which "specific" grammatically modifies. However, it is not apparent what such a limitation might be in each instance.

Regarding claim 6, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

In claim 7, "cites" should be "sites".

Claim 10 recites "a hybrid gene selected from the group consisting of" several pairs of genes. However, this format is confusing, as it is not clear if the genes are set forth as associated pairs, as parts of the hybrid, or as a single, continuous list. It is suggested that the language of claim 7 of US Patent 5,998,382 be employed, "pairs of DNA sequences in operable linkage".

Claim 11 places a period after "3 cm", followed by capitalization of the next word "Distant".

Certain papers related to this application may be submitted to the directly to the Examiner by facsimile transmission at (703) 746-5155. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993)(see 37 CFR ' 1.6(d)). To send the facsimile to the Art Unit instead, the Art Unit 1636 Fax number is (703) 305-7939. NOTE: If Applicant does submit a paper by fax to this number, the Examiner must be notified promptly, to ensure matching of the faxed paper to the application file, and the original signed copy should be retained by Applicant or Applicant's representative. (703) 308-4242 or (703) 305-3014 may be used without notification of the Examiner, with such faxed papers being handled in the manner of mailed responses. Applicant is encouraged to use the latter two fax numbers unless immediate action by the Examiner is required, e.g., during discussions of claim language for allowable subject matter. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the Examiner with respect to the examination on the merits should be directed to James Ketter whose telephone number is (703) 308-1169. The Examiner normally can be reached on M-F (9:00-6:30), with alternate Fridays off.

Questions regarding formalities and processing of the case should be directed to Zeta Adams, whose telephone number is (703) 305-3291.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Remy Yucel, can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Jsk
October 31, 2002

JAMES KETTER
PRIMARY EXAMINER